

## **REMARKS**

Reconsideration of this application, as amended, is respectfully requested.

The Applicants wish to draw the Examiner's attention to the Applicants' related co-pending applications and issued patents (see Appendix A) directed to nanoparticles and methods of preparation and use thereof. Many office actions have already issued for these cases; a number of cases have already granted.

The Applicants note that the Examiner did not return executed copies of the PTO 1449 form for the 6<sup>th</sup> Supplemental IDS that was hand delivered to the Examiner on September 9, 2002. The Applicants request that the Examiner fully execute the PTO 1449 form for the 6<sup>th</sup> Supplemental IDS and return a copy of the executed PTO 1449 form to the undersigned representative. A copy of the 6<sup>th</sup> Supplemental IDS, associated PTO 1449 form, and PTO stamped postcard acknowledging receipt of the IDS, PTO 1449 form and references are attached. The Examiner is requested to contact the undersigned representative if the Examiner would like to have another copy of the references.

The specification was amended to update the priority claim, thus obviating the Examiner's objection to the specification. No new matter has been introduced by this amendment.

Claims 243-265, 267, 291-336, 360-406, 422, 426, 428, 430, and 432-444 were pending in this application and were subject to a restriction requirement. The Applicants had elected the claims of Group I (claims 243-265, 422, 430, and 433-444) for prosecution purposes. In this amendment, non-elected claims 267, 291-336, 360-406, 426, 428, and 432 were cancelled without prejudice or disclaimer in order to expedite the prosecution of this application. In addition, the informalities in claims 252 and 430 were corrected as requested by the Examiner. Support for the amendments and new claims can be found in the original claims and in the specification, e.g., pages 77-80. Cancelled claims 422 and 430 were renumbered as claims 445 and 446, respectively. Accordingly, no new matter has been introduced into this application as a result of the present amendment. Claims 243-265, and 433-445 are pending in this application.

Turning to the office action, claims 243-265, 422 (now claim 444) and 430 (now claim 445) were rejected under 35 U.S.C. section 102(e) as being anticipated by or, in the alternative,

under 35 U.S.C. section 103(a) as obvious over Yguerabide (U.S. Patent No. 6,214,560)("Yguerabide"). The Applicants respectfully traverse these rejections.

As a general rule, for prior art to anticipate under section 102, every element of the claimed invention must be identically disclosed in a single reference. Corning Glass Works v. Sumitomo Electric, 9 U.S.P.Q.2d 1962, 1965 (Fed. Cir. 1989). The exclusion of a claimed element, no matter how insubstantial or obvious, from a reference is enough to negate anticipation. Connell v. Sears, Roebuck & Co., 220 U.S.P.Q 193, 1098 (Fed. Cir. 1983). Applicants respectfully submit that Yguerabide cannot be applied to support an anticipation rejection of claims 243-265 and 433-445 under 35 U.S.C. section 102(e).

Likewise, the Federal Circuit reiterated the manner in which obviousness rejections are to be reviewed. Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, "a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success." *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991), citing *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q. 2d 1529, 1531 (Fed. Cir. 1988). Applicants respectfully submit that Yguerabide does not teach or suggest the Applicants' invention as presently claimed.

Specifically, the Examiner alleged that Yguerabide taught detection and measurement of one or more analytes in a sample using particles of specific composition and size using light scattering. The discussion is found starting in col. 82, line 35, of Yguerabide. Col. 83 provides further discussion regarding particle size and particle binding to a surface. Contrary to the Examiner's position, there is no discussion anywhere in Yguerabide of any nanoparticle probe capable of forming hybridization complexes having sharp melting profiles, increased melting temperatures, and extraordinary discrimination properties. The nanoparticle-labeled probes of the present invention form complexes, under hybridization conditions, with target nucleic acids or other oligonucleotides and the resulting complexes have sharp melting profiles and increased melting temperatures. These properties allow for extraordinary discrimination between perfectly matched and mismatched nucleic acid targets relative to complexes including unlabeled or

fluorophore-labeled oligonucleotides. For instance, as shown in Figure 12 and discussed in Example 5 (page 90 in the specification, nanoparticle labeled oligonucleotide probes were prepared and contacted with various target nucleic acids under stringent conditions. With fully matched targets, the complex produced a positive result (blue color); with targets having one mismatched base, no complex formation occurred with the probes. In Figure 35(b), dehybridization of nanoparticle – labeled targets from capture strands bound to a surface was much more sensitive to temperature than that of an analogous fluorophore-labeled targets with identical sequences (Figure 35(a)). In addition, Figure 36 shows images of model oligonucleotide arrays challenged with unlabeled synthetic target and fluorescent-labeled (Figure 36(a)) or nanoparticle-labeled (Figure 36(b)) probes. That Figure showed that arrays challenged with model target and nanoparticle labeled probes and stained with silver solution clearly exhibited highly selective hybridization to complementary array elements and that the selectivity of the nanoparticle-based arrays was higher than that of the fluorophore-indicated arrays. See also the specification at page 135, lines 12-28. The claimed nanoparticles are neither taught, made obvious, or suggested by Yguerabide. Accordingly, withdrawal of the section 102(e) rejection of the claims based on Yguerabide is in order and is respectfully requested.

Finally, claims 243-265 stand provisionally rejected under 35 U.S.C. section 101 as claiming the same invention as that of claims 243-265 of co-pending application no. 09/974,007 (the '007 application). In light of the present amendment, the Applicant believes that the double patenting rejection based on the '007 application does not apply. Withdrawal of the double patenting rejection is in order and is respectfully requested.

In conclusion, the Applicants respectfully submit that the claims in this application are in allowable condition and request a Notice to this effect.

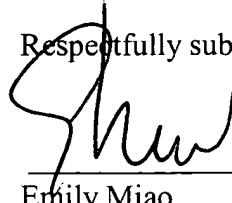
Reconsideration of this application is respectfully requested and a favorable determination is earnestly solicited. The Examiner is invited to contact the undersigned

representative if the Examiner believes that this would be helpful in expediting the prosecution of this application.

Dated: 1/13/04

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Respectfully submitted,



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Page 1 of 6

## APPENDIX A

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
00-653-A	U.S. 09/927,777 Filed 8/10/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton, Garamella, Li, Park/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFORE	ALLOWED
00-713-B1	09/923,625 Filed 8/7/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFOR	PENDING
00-713-C	09/344,667, filed 6/25/99	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFORE	U.S. Patent No. 6,361,944, issued 3/26/02
00-713-I	U.S.S.N 09/603,830 Filed 6/26/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFOR	U.S. Patent No. 6,506,564, issued 1/14/03
00-713-I-1	09/961,949 9/20/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton;	U.S. Patent No. 6,582,921, issued June 24, 2003

<b>ATTY Case No.</b>	<b>Serial No./ Filing Date</b>	<b>Inventors/Title</b>	<b>Status</b>
		NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFOR	
<b>00-713-I-2</b>	09/957,318 9/20/01	See 00-713-I-1	ALLOWED
<b>00-713-I-3</b>	09/957,313 9/20/01	See 00-713-I-1	U.S. Patent No. 6,645,721, issued 11/11/03
<b>00-713-I-4</b>	09/966,491 9/28/01	See 00-713-I-1	U.S. Patent No. 6,610,491, issued August 26, 2003
<b>00-713-I-5</b>	09/966,312 9/28/01	See 00-713-I-1	U.S. Patent No. 6,673,548, issued January 6, 2004
<b>00-713-I-6</b>	09/967,409 9/28/01	See 00-713-I-1	ALLOWED
<b>00-713-I-7</b>	09/974,500 10/10/01	See 00-713-I-1	ALLOWED
<b>00-713-I-8</b>	09/974,007 10/10/01	See 00-713-I-1	PENDING
<b>00-713-I-9</b>	09/973,638 10/10/01	See 00-713-I-1	PENDING
<b>00-713-I-10</b>	09/973,788 10/10/01	See 00-713-I-1	ALLOWED
<b>00-713-I-11</b>	09/975,062 10/11/01	See 00-713-I-1	U.S. Patent No. 6,677,122, issued January 13, 2004
<b>00-713-I-12</b>	09/975,376 10/11/01	See 00-713-I-1	PENDING
<b>00-713-I-13</b>	09/975,384 10/11/01	See 00-713-I-1	PENDING

<b>ATTY Case No.</b>	<b>Serial No./ Filing Date</b>	<b>Inventors/Title</b>	<b>Status</b>
<b>00-713-I-14</b>	09/975,498 10/11/01	See 00-713-I-1	ALLOWED
<b>00-713-I-15</b>	09/975,059 11/11/01	See 00-713-I-1	PENDING
<b>00-713-I-16</b>	09/976,601 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-17</b>	09/976,968 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-18</b>	09/976,971 10/12/01	See 00-713-I-1	ALLOWED
<b>00-713-I-19</b>	09/976,863 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-20</b>	09/976,577 10/12/01	See 00-713-I-1	ALLOWED
<b>00-713-I-21</b>	09/976,618 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-22</b>	09/981,344 10/15/01	See 00-713-I-1	ALLOWED
<b>00-713-I-23</b>	09/976,900 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-24</b>	09/976,617 10/12/01	See 00-713-I-1	ALLOWED
<b>00-713-I-25</b>	09/976,378 10/12/01	See 00-713-I-1	PENDING
<b>00-713-i-26</b>	10/410,324 04/10/03	See 00-713-I-1	PENDING
<b>00-713-L</b>	U.S.S.N. 09/693,005 Filed 10/20/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI	U.S. Patent No. 6,495,324, issued 12/17/02

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
		DES ATTACHED THERETO AND USES THEREFORE	
<b>00-713-M</b>	U.S.S.N. 09/693,352 Filed 10/20/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND USES THEREFORE	U.S. Patent No. 6,417,340, issued 7/9/02
<b>00-714-G</b>	U.S. 09/830,620 Filed 8/15/01	Mirkin, Nguyen/ NANOPARTICLES WITH POLYMER SHELLS	PENDING
<b>00-715-A</b>	U.S. 09/760,500 Filed 1/12/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; Garamella, Li/ METHOD OF ATTACHING OLIGONUCLEOTI DES TO NANOPARTICLES AND PRODUCTS PRODUCED THEREBY	ALLOWED
<b>00-1085-A</b>	U.S.S.N. 09/820,279 Filed 3/28/01	Mirkin, Letsinger, etc./ METHOD AND MATERIALS FOR ASSAYING BIOLOGICAL MATERIALS	ALLOWED
<b>00-1085-G</b>	U.S.S.N. 10/640,618 Filed 8/13/03	Mirkin, Letsinger, etc./ METHOD AND MATERIALS FOR ASSAYING BIOLOGICAL MATERIALS	PENDING
<b>00-1086-A</b>	U.S. 09/903,461 Filed 7/11/01	Letsinger, Garimella/ METHOD OF DETECTION BY ENHANCEMENT	U.S. Patent No. 6,602,669, Filed 8/5/03



ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
		OF SILVER STAINING	
00-1272-C	U.S.S.N. 10/008,978 Filed 12/7/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton, Garimella, Li, Park, Lu/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREOF	PENDING
01-565-A	USSN 10/125,194 Filed 4/18/02	Mirkin, Nguyen, Watson, Park/ OLIGONUCLEOTI DE-MODIFIED ROMP POLYMERS AND CO- POLYMERS	PENDING
01-599-A	U.S.S.N. 10/291,291 Filed 11/08/02	Storhoff/NOVEL THIOL-BASED METHOD FOR ATTACHING OLIGONUCLEOTI DES TO NANOPARTICLES	PENDING
01-661-A	U.S.S.N. 10/034,451 Filed 12/28/01	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
01-661-C	U.S.S.N. 10/153,483 Filed 5/22/02	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
01-661-E	U.S.S.N. 10/397,579 3/26/03	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
01-1565-A	U.S.S.N. 10/266,983	Park, Taton, Mirkin/ARRAY-	PENDING

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
	Filed 10/08/02	BASED ELECTRICAL DETECTION OF DNA USING NANOPARTICLE PROBES	
<b>01-1633-A</b>	U.S.S.N. 10/266,983 Filed 10/8/02	Park, Taton, Mirkin/NANOPARI CLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFOR	PENDING
<b>01-1705-A</b>	U.S.S.N. 10/108,211 Filed 3/27/02	Nam, Park, Mirkin/BIO- BARCODES BASED ON OLIGONUCLEOTI DE-MODIFIED NANOPARTICLES	PENDING
<b>02-338-B</b>	USSN 10/172,428 Filed 6/14/02	Cao, Jin, Nam, Mirkin/MULTIHA NNEL DETECTION USING NANOPARTICLE PROBES WITH RAMAN SPECTROSCOPIC FINGERPRINTS	PENDING
<b>02-338-C</b>	10/431,341 5/7/03	Cao, Jin, Nam, Mirkin/MULTIHA NNEL DETECTION USING NANOPARTICLE PROBES WITH RAMAN SPECTROSCOPIC FINGERPRINTS	PENDING